GUIDED READING - *Ch. 18 – REGULATION OF GENE EXPRESSION* **NAME:** _____

- **Please print out these pages and HANDWRITE the answers directly on the printouts.** *Typed work or answers on separate sheets of paper will not be accepted.*
- **Importantly, guided readings are NOT GROUP PROJECTS!!!** *You, and you alone, are to answer the questions as you read. You are not to share them with another students or work together on filling it out. Please report any dishonest behavior to your instructor to be dealt with accordingly.*
- **Get in the habit of writing legibly, neatly, and in a NORMAL, MEDIUM-SIZED FONT.** *AP essay readers and I will skip grading anything that cannot be easily and quickly read so start perfect your handwriting.*
- **Please SCAN documents properly and upload them to Archie.** *Avoid taking photographs of or uploading dark, washed out, side ways, or upside down homework. Please use the scanner in the school's media lab if one is not at your disposal and keep completed guides organized in your binder to use as study and review tools.*
- **READ FOR UNDERSTANDING and not merely to complete an assignment.** *Though all the answers are in your textbook, you should try to put answers in your own words, maintaining accuracy and the proper use of terminology, rather than blindly copying the textbook whenever possible.*

"WHILE ALL CELLS OF AN ORGANISM HAVE ALL GENES IN THE GENOME, NOT ALL GENES ARE EXPRESSED IN EVERY CELL. Furthermore, gene expression in prokaryotic cells differ from that in eukaryotic cells and, in multi-cellular eukaryotes, the disruption in gene regulation can lead to cancer." [2]

Bacteria often respond to environmental change by regulating transcription [2].

1. All genes are not "on" all the time. Using the metabolic needs of E. coli, explain why not. [2]

2. Cells intricately and very precisely regulate their gene expression. Prokaryotes and eukaryotes alter their pattern of gene expression in response to change in environmental conditions. Multicellular organisms also need to maintain many different types of cells each with the same copy of DNA but expressing different genes. Briefly describe **the two levels at which metabolic control occurs?** Which is considered a rapid response and which a slower more long-term response to changes in the environment?

   a.

   b.

3. Feedback inhibition is a recurring mechanism throughout biological systems. **In the case of E. coli regulating tryptophan synthesis, is it positive or negative inhibition**? Explain your choice. [2]

4. What is a **promoter**?

5. First we will look into **PROKARYOTIC gene control**. *E. coli* synthesizes the amino acid tryptophan in a multi-step pathway in which each step is catalyzed by a specific enzyme. The five genes that code for these enzymes are clustered together on the bacterial chromosome as part of an operon. What is an **operon**?

6. List the **three components of an operon**. Explain the role of each one.

   a.

   b.

   c.

7. What is an **operator** and where is it located?

8. In E. coli, **a SINGLE promoter serves all five genes that code for the tryptophan synthesizing enzymes, which together constitute a transcription unit.** Transcription gives rise to one long mRNA molecule that codes for the five polypeptides making up the enzymes in the tryptophan pathway. What is a **major benefit of grouping genes with related function into one transcription unit**?

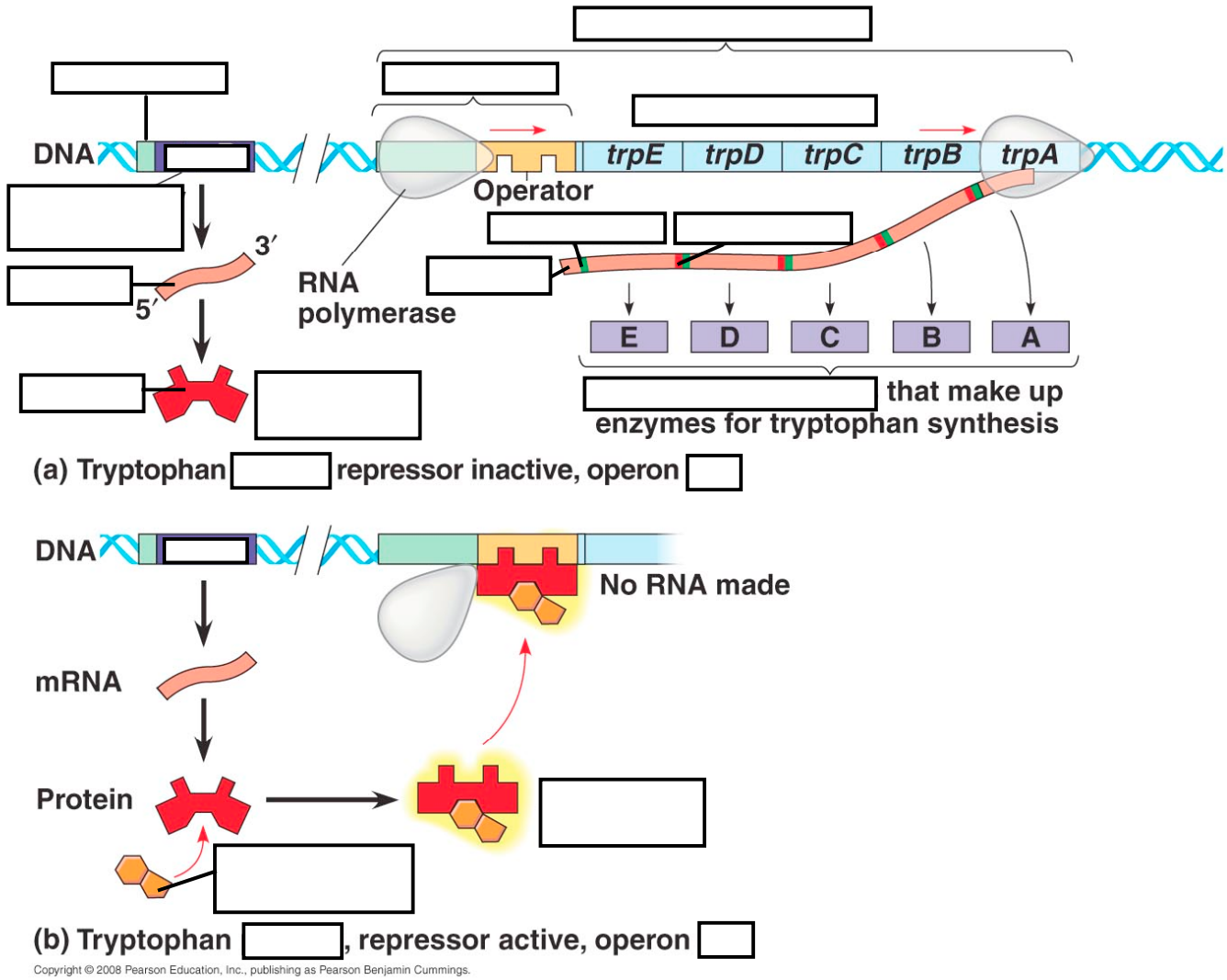
9. How does a **repressor protein** work? [2]

10. What are **regulatory genes**? [2]

11. a. Distinguish between **inducible and repressible operons**.

b. Briefly describe one example of each.

12. Lets focus on **the trp operon in E. coli** which allows the in the tryptophan pathway to respond to changes in tryptophan availability in the environment. Carefully read the section Operon: The Basic Concept and study figure 18.3 before continuing. Next, label the illustration of the trp operon and operon regulation.



13. Now try to answer these on your own...

    a. What are the **final products of the genes that are a part of the trp operon**?

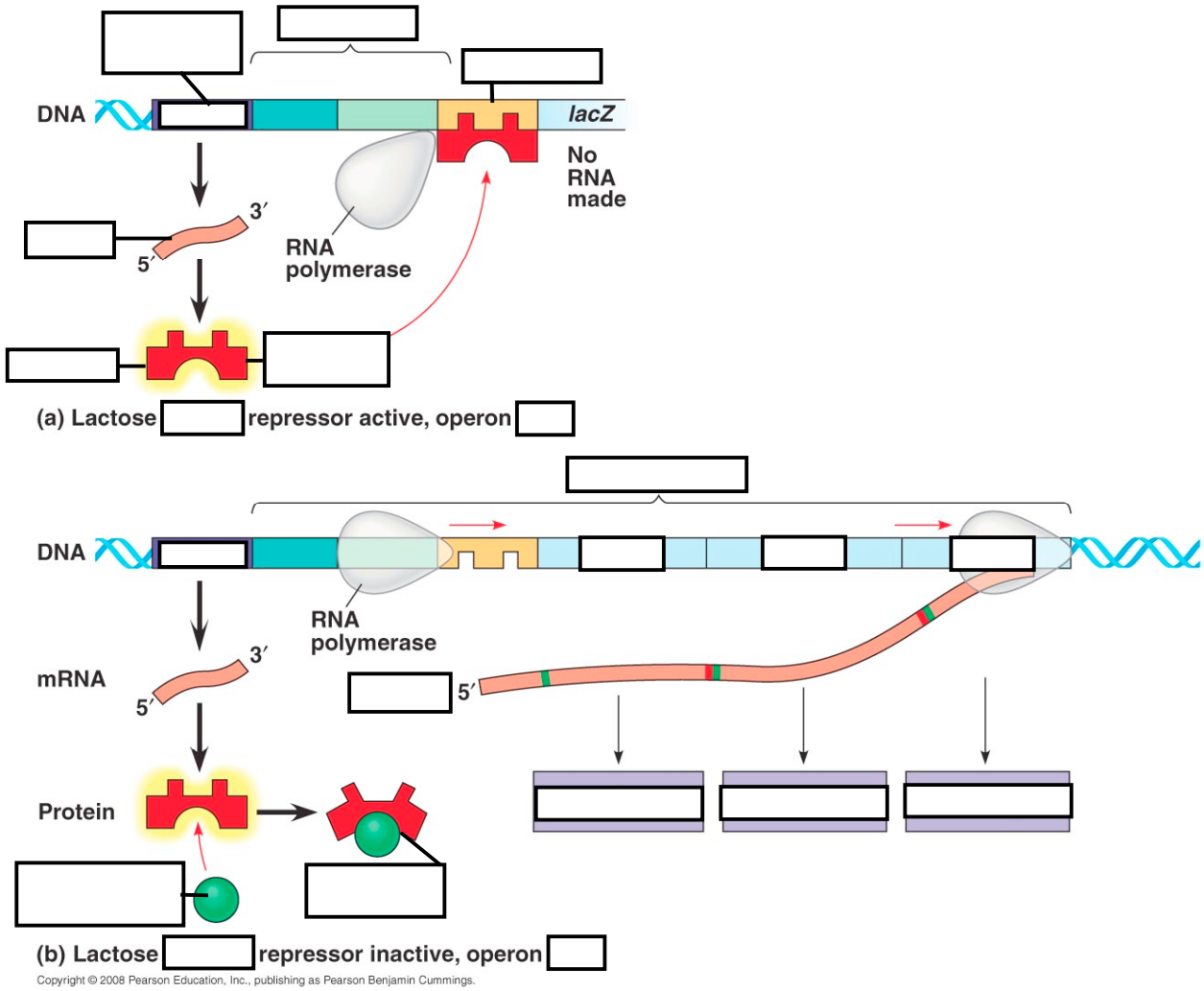
    b. How exactly is the **operon switched off**?

    c. **What makes the trp repressor**?

    d. Detail **trp repressor's role in turning off the operon**, being sure to include a discussion on the role **tryptophan plays as a corepressor**?

14. NEGATIVE GENE REGULATION: **Operons are switched OFF by the active form of the repressor protein**. The **trp operon is a repressible operon**, its transcription is always on but it can be inhibited (repressed) when a small molecule like tryptophan binds allosterically to a regulatory protein.

    By contrast, the **lac operon is an inducible operon**, usually off but stimulated (induced) by a small molecule interacting with a regulatory protein. Read the section on the lac operon and carefully study figure 18.4. Then label the figure showing the lac operon and its regulation.



15. a. The lac operon includes the genes (*lacZ, lacY, lacA*) that code for three enzymes involved in lactose utilization. What is the **function of the product of the *LacZ* gene product β–galactosidase**?

    a. What is the purpose of the ***lacI* regulatory gene** and what is **the function of the protein it codes for**?

    b. Define the term **inducer**.

    c. Explain how **allolactose functions as an inducer of the lac operon**.

16. **POSITIVE GENE REGULATION: Transcription is switched ON by a regulatory protein**.

    E. coli prefers to use _____ as its source of energy, breaking it down in glycolysis. **Only when lactose Is available AND glucose absent does E. coli use lactose as an energy source**.

17. Lets review now... **Compare and contrast the lac operon and the trp operon**. *(Remember that COMPARE means "to tell how they are similar" and CONTRAST means "to tell how they are different.")*

    Compare

    Contrast

18. What happens when a **repressor** is bound to the *lac* operon's operator? [2]

19. What is an **activator**?

20. a. Would *E.coli* preferentially use glucose or lactose if BOTH glucose and lactose concentrations were high in the cells environment?

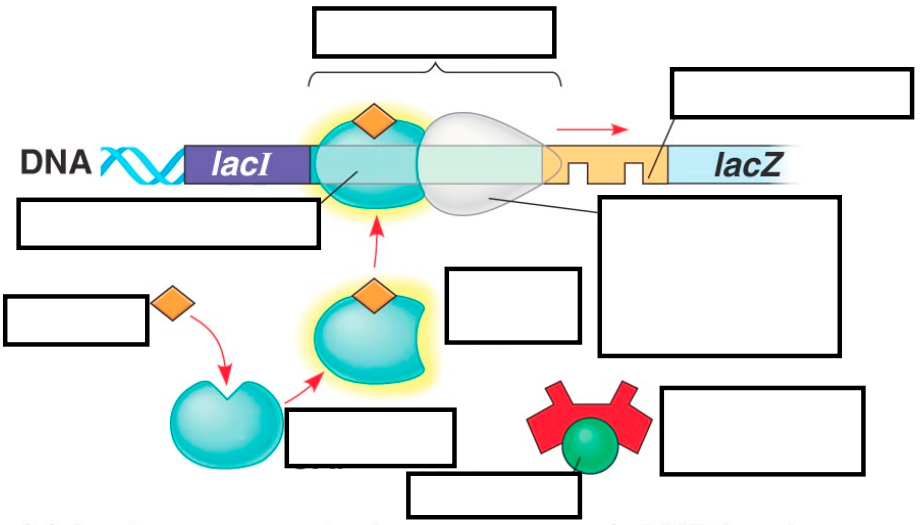
    b. Comment on the **transcription rate of the *lac* operon when both glucose and lactose are present**. Why is the rate as it is…?

21. a. What is **CAP**? [2]

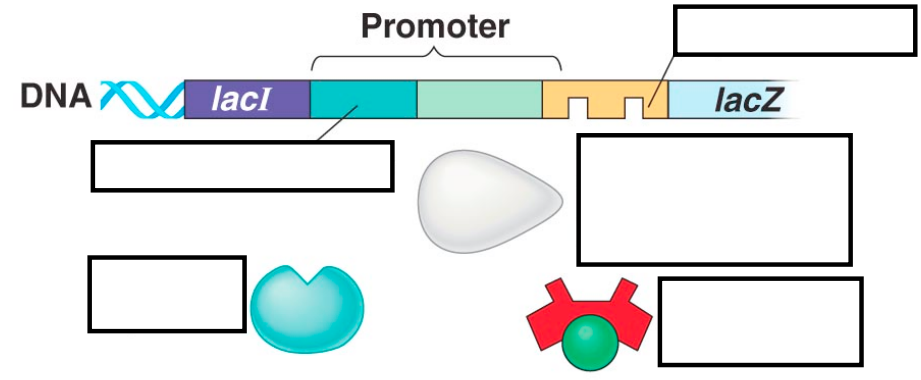
    b. How does CAP work? [2]

c. The ***lac* operon is under both positive and negative control**. In **negative control, the lac repressor binds to the operator** when no lactose is present in the cell. Explain why **CAP binding and stimulation of gene expression is positive regulation**. [2]

d. Label the figure below showing the effect of **CAP activation and inactivation** on *lac* operon transcription.



(a) Lactose present, glucose scarce (cAMP level high): _____ *lac* mRNA synthesized



(b) Lactose present, glucose present (cAMP level low): _____ *lac* mRNA synthesized

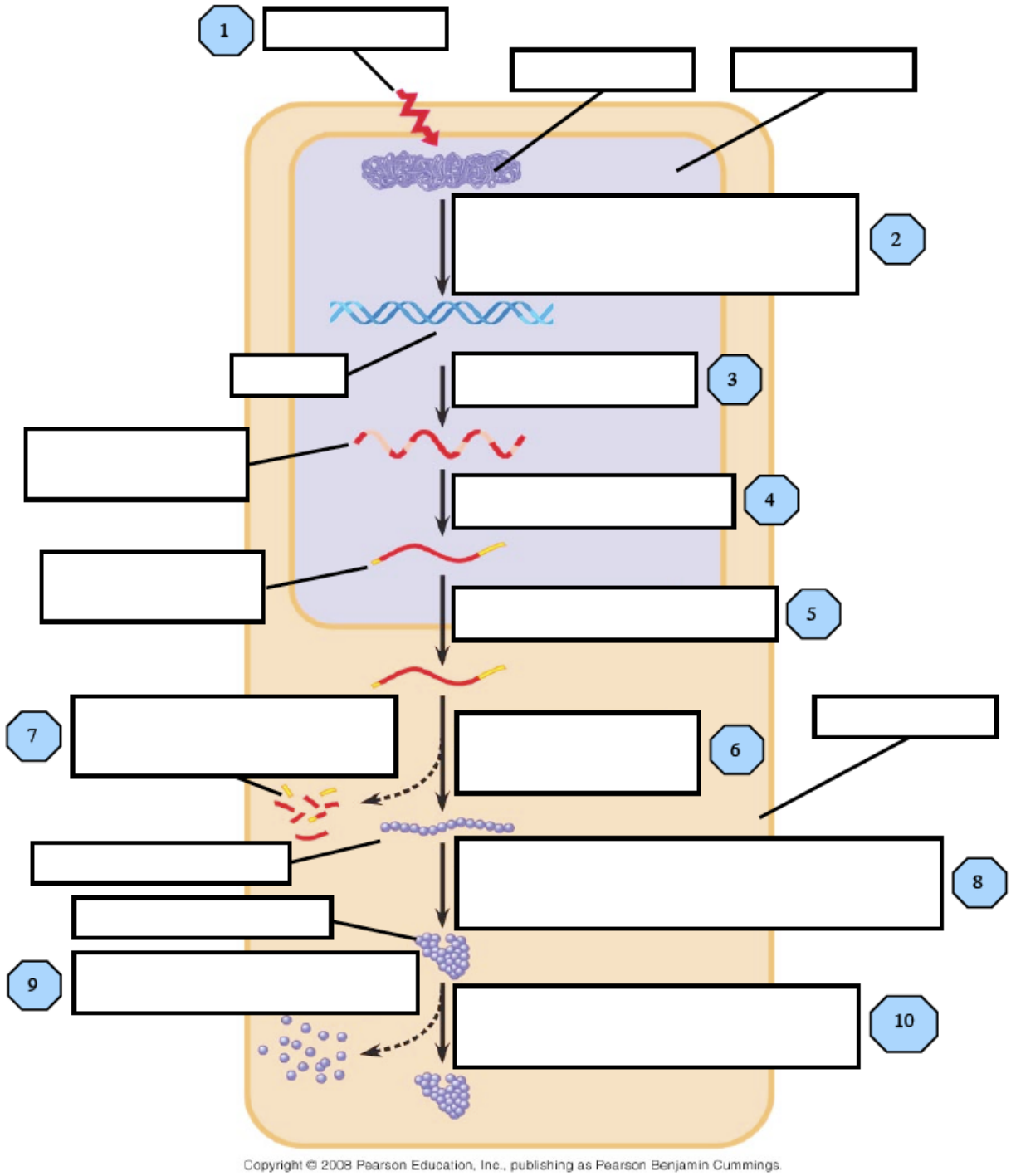
22. Putting the whole picture together, describe in your own words the **relationship between glucose supply, camp, and CAP**. [2]

Eukaryotic gene expression can be regulated at any stage *[2].*

23. Even though all cells of an organism have the same genes, a **typical human cell probably expresses about 20% of its genes at any given time**, leading to differential gene expression. What is meant by '**differential gene expression**'?

24. a. In all organisms, prokaryotes and eukaryotes, what is the **common control point of gene expression**? [2]

b. Eukaryotic cells have a structure that provides additional opportunities for regulating gene expression. Label the diagram below listing the **10 stages of gene expression in eukaryotes that can serve as points of Regulation**



25. **Chromatin not only packs DNA into a compact form that fits inside the nucleus but also helps regulate gene expression in several ways.** The location of a gene's promoter relative to nucleosome and to the sites where the DNA attaches to the chromosome scaffold or nuclear lamina can affect whether a gene is transcribed.

    a. Are genes within **heterochromatin or euchromatin** usually expressed?

    b. Distinguish between the structure of heterochromatin and euchromatin and how does this structure help control gene expression.

26. **Chemical modifications of histones** can influence chromatin structure and gene expression. What end of the histone amino acid sequence normally gets modified?

27. a. What occurs in **histone acetylation**?

    b. What effect does **histone acetylation** have on gene expression? Why?

    c. What effect does **histone deacetylation** have on gene express? Why?

28. a. What occurs in **DNA methylation**?

    c. What role may it play in gene expression?

d. The **inactivate mammalian X chromosome** (bar body) is heavily methylated. What is the result of this methylation?

e. What is **genomic imprinting** and how is it maintained? [2]

29. Explain what is meant by **epigenetic inheritance**, and give an example of epigenetic changes discussed in the text, in documentaries, or in class. [2]

30. **Chromatin-modifying enzymes provide initial control of gene expression** by making a region of DNA either more or less able to bind the transcription machinery. Once the chromatin of a gene is optimally modified for expression, the **initiation of transcription is the next major step at which gene expression is regulated**. These involve proteins that bind to DNA and either facilitate or inhibit binding of RNA polymerase.

a. What are '**control elements'**?

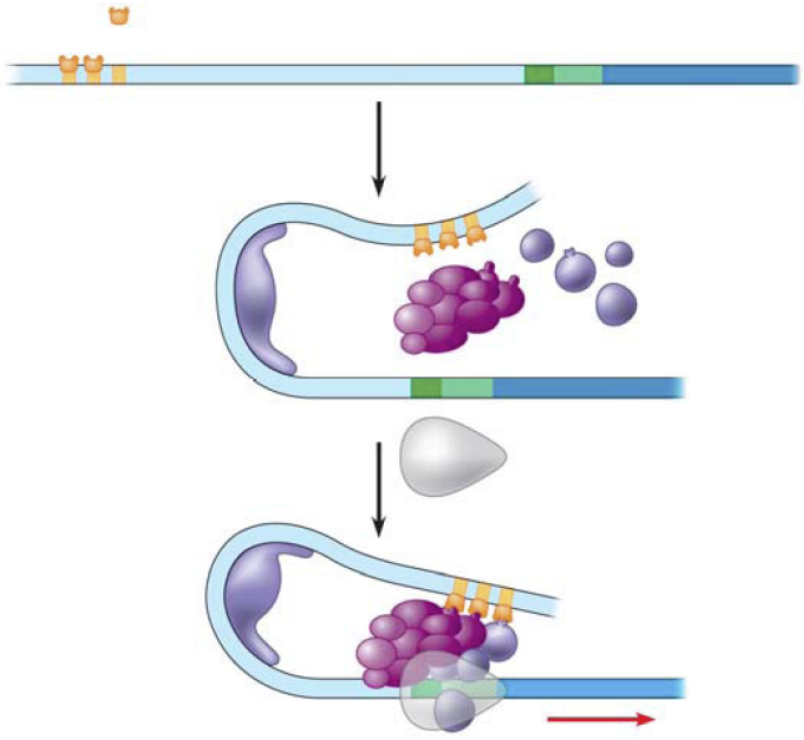
b How are **general transcription factors** and **specific transcription factors** similar and different?

c. What are '**enhancers**'?

d. What are '**activators**' and how do they affect gene expression?

e. What are '**repressors**' and how do they affect gene expression?

31. a. On average, **<u>each enhancer is composed of about ten control elements</u>**, each of which can bind only one or two specific transcription factors. **The specific transcription factors made in a cell determines which genes are expressed in that cells.** First, label the diagram below with the following elements: *TATA box, promoter, gene, enhancer, activators, general and specific transcription factors, transcription initiation complex, RNA polymerase II, DNA, proximal and distal control elements, DNA bending protein, and mediator proteins*.



b. Next, use the diagram to explain how **enhancers and transcription activators interact with transcription factors to affect gene expressions**.

32. **In prokaryotes, functionally related genes are usually clustered together in a single operon**. Operons have not been found in eukaryotic cells, and the genes coding for the enzymes of a particular metabolic pathway are often scattered over different chromosomes. What has been found to be the **case in eukaryotes in relation to coordinate control mechanisms**?

33. Suppose you compared the nucleotide sequence of the distal control elements in the enhancers of three genes that are expressed only in muscle tissue. What would you expect to find? Why? [1]

33. Once mRNA encoding a particular protein reaches the cytoplasm, list the four mechanisms that can regulate the amount of the protein that is active in the cell? [1]

a.

b.

c.

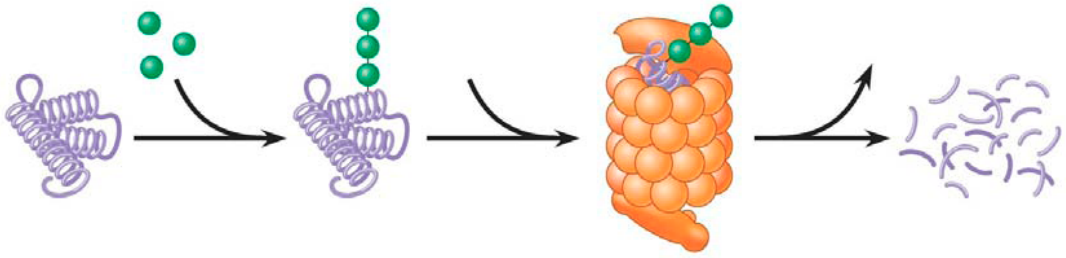
d.

34. Explain how **RNA processing's <u>Alternative RNA Splicing</u>** is a mechanism of **<u>post-transcriptional gene regulation, resulting in different proteins derived from the same initial RNA transcript</u>**. [2]

35. Posttrancriptional control includes regulation of mRNA degradation. <u>How</u> does **<u>mRNA Degradation</u>** and the **<u>prevention of translation initiation</u>** affect translation and gene expression?

36. How can proteins be activated, processed, and degraded? *Give an example or describe each process. [2]*

37. An article in Scientific American about proteasomes was entitled "Little Chambers of Horrors." [2] Explain how What are '**proteasomes**' and how do they work? *Label the illustration below as part of your answer and use it to explain their activity.*



38. Explain the **proteasomes' role in regulating gene expression**. [2]

Noncoding RNAs play multiple roles in controlling gene expression [2].

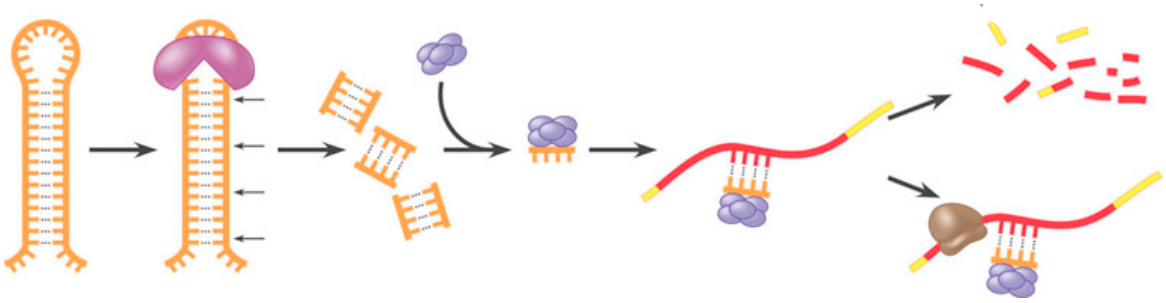
39. How much of the **human genome appears to code for proteins**?

40. It is now known that much of the RNA that is transcribed is not translated into protein. What two crucial things seem to be **regulated by noncoding RNAs, helping control eukaryotic gene expression**?

    1.

    2.

41. a. Often the **noncoding RNAs that regulate gene expression is microRNA**. Label the following illustration and use it to explain how **miRNA-protein complexes are made** in eukaryotes.



b. Explain the **two modes of action of microRNAs (miRNA's) in post-transcriptional regulation**.

1.

2.

42. Imagine that the mRNA being degraded in Figure 18.13 codes for a protein that promotes cell division in a multicellular organism. What would happen, both in the cell and to the organism, if a mutation disabled the gene encoding the miRNA that triggers this degradation? [1]

A program of differential gene expression leads to the different cell types in a multicellular organism [2].

43. What **three processes lead to the transformation of a zygote into the organism**? [2]

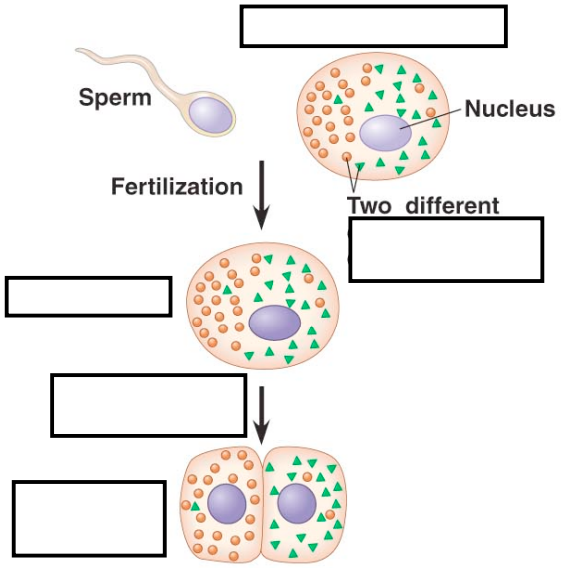
    1.

    2.

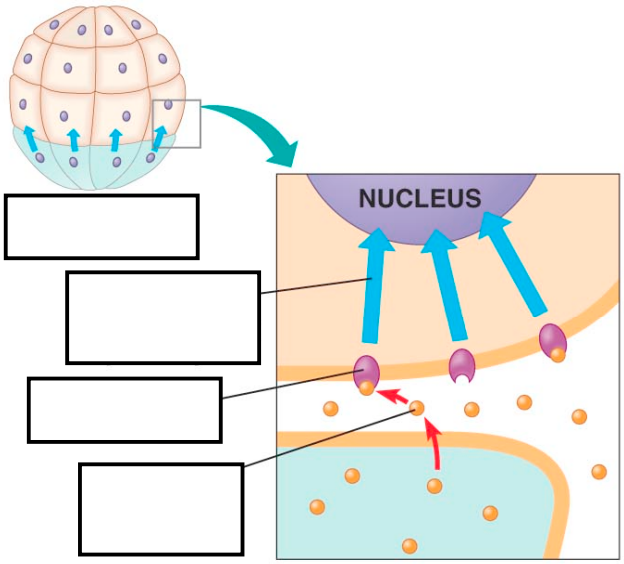
    3.

44. What is '**cell differentiation**' and how does that relate to '**morphogenesis**'?

45. Explain the roles of the following **two important sources of information in early embryonic development that lead to specific genes being expressed in one cell and not another**, allowing cells to develop along particular and distinct paths? Be sure to label the figure below and include definitions of **cytoplasmic determinants** and **induction** in your explanations.



(a) Cytoplasmic determinants in the egg



(b) Induction by nearby cells

46. What is meant by **determination**? *Explain what this means within an embryonic cell.* [2]

47. a. What **process ensures that all the tissues and organs of an organism are in their characteristic places**? [2]

b. Where do the **molecular cues** that control this process arise? [2]

48. What is controlled by **homeotic genes**? [2]

Cancer results from genetic changes that affect cell cycle control [2].

49. a. What is the difference between **oncogenes** and **proto-oncogenes**?

b. List & DESCRIBE **the three genetic changes (mechanisms) that can that can convert a proto-oncogene into an oncogene**.

1.

2.

3.

50. There seem to be two categories of genes involved in cancer: ***ONCOGENES*, which code for proteins to regulate cell growth, and should not be stuck "on," much like the accelerator in a car; and *TUMOR-SUPPRESSOR GENES*, which work like the brakes on a car and must function!** What exactly are '**tumor-suppressor genes**' & what role can they play in the onset of cancers?

51. ***The proteins encoded by many proto-oncogenes and tumor-suppressor genes are components of the cell signaling pathways.*** Interference with normal signaling pathways then seems to be an important factor in cancer development. Mutations in the ras proto-oncogene, which codes for a G protein, occur in about 30% of human cancers while mutations in the p53 tumor-suppressor gene, accounts for more than 50% of cancers.

a. What is the importance of the **ras gene**?

b. Is a functioning **ras gene an oncogene or proto-oncogene**? Why?

c. What is the importance of the **p53 gene** sometimes called the "guardian angel of the genome?"

d. Why is the **p53 gene considered a tumor-suppressor gene**?

e. In what **three ways does p53 protein prevent cells from passing on mutations due to DNA damage**?

1.

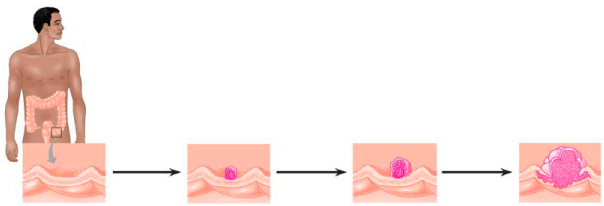
2.

3.

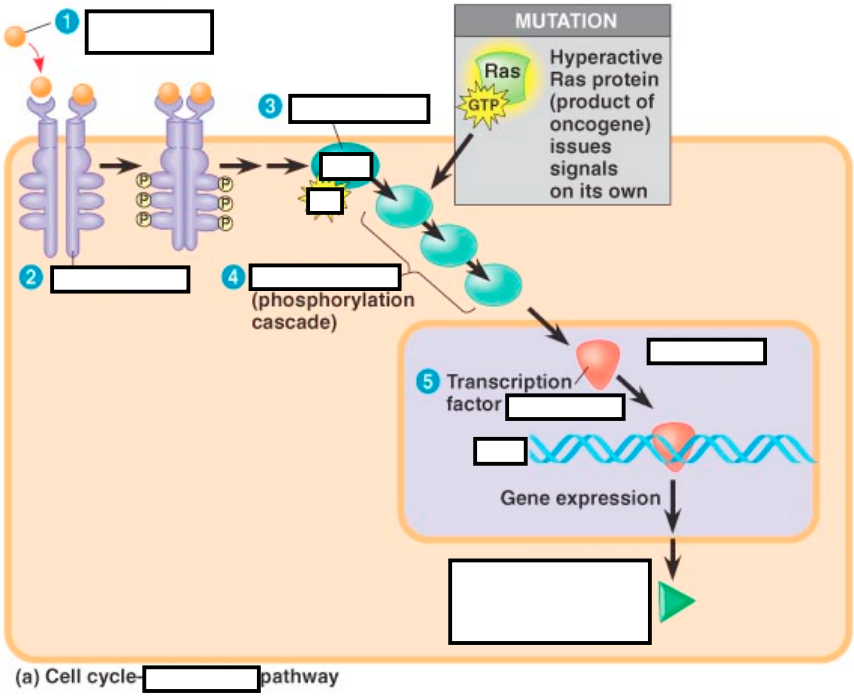
52. How many changes must occur at the DNA level for a typical cell to become fully cancerous?

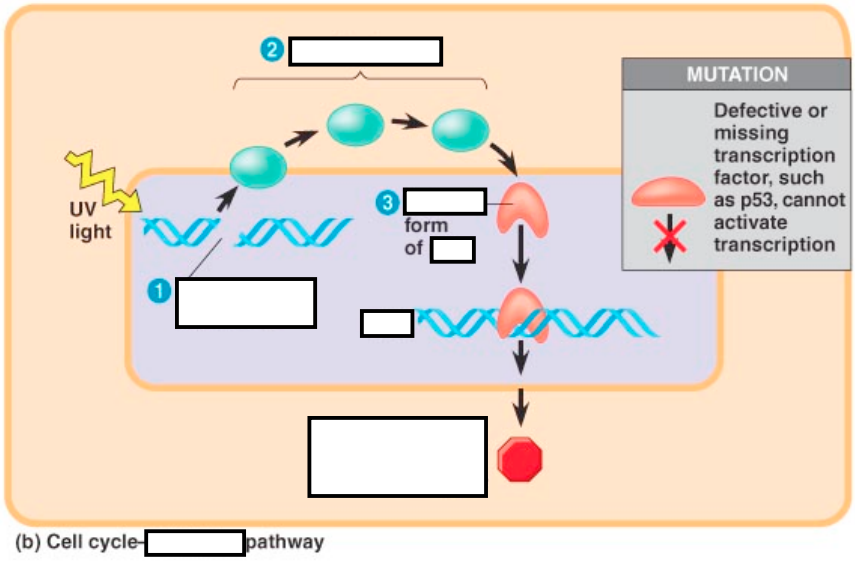
53. Why is said that **people inherit predispositions to cancer not cancer itself**? [3]

54. Explain the ***multistep model of cancer development*** by using the specific example of colorectal cancer. *The figure below may be labeled to help in your explanation.* [2]



55. **Stimulatory and inhibitory pathways regulate the cell cycle**, commonly by **influencing transcription**. Label the diagrams and briefly describe **the signaling pathways that regulate cell division and how aberrations in such pathways can lead to cancer**.





56. Please answer the Self-Quiz at the end of your chapter. *Do your best to try it from memory first in order to test how well you grasped the material.*

1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____ 7. _____ 8. _____ 9. _____ 10. _____

References

1. Campbell *et al*. (2008). AP* Edition Biology. 8th Ed. San Francisco: Pearson Benjamin Cummings.
2. Adapted from Fred and Theresa Holtzclaw
3. Adapted from L. Miriello